

ABSTRACT

Objectives

To compare the acute perceptual and blood pressure responses to: 1) light load blood flow restriction resistance exercise (BFR-RE) in non-injured individuals and anterior cruciate ligament reconstruction (ACLR) patients; and 2) light load BFR-RE and heavy load RE (HL-RE) in ACLR patients.

Design

Between-subjects, partially-randomised.

Methods

This study comprised 3 groups: non-injured BFR-RE (NI-BFR); ACLR patients BFR-RE (ACLR-BFR); ACLR patients HL-RE (ACLR-HL). NI-BFR and ACLR-BFR performed 4 sets (30, 15, 15, 15 reps, total=75 reps, 30s inter-set rest) of unilateral leg press exercise at 30% 1RM with continuous BFR at 80% limb occlusive pressure. ACLR-HL performed 3 x 10 reps (Total=30 reps, 30s inter-set rest) of unilateral leg press exercise at 70% 1RM. Perceived exertion (RPE), muscle pain, knee pain and pre- and 5-min post-exercise blood pressure were measured.

Results

RPE was higher in ACLR-BFR compared to NI-BFR ($p<0.05$). Muscle pain was higher in NI-BFR and ACLR-BFR compared to ACLR-HL ($p<0.05$). Knee pain was lower in ACLR-BFR compared to ACLR-HL ($p<0.01$). There were no differences in blood pressure.

Conclusion

These responses to BFR exercise may not limit application and favourably influence knee pain throughout ACLR rehabilitation training programmes. These findings can help inform practitioners' decisions to utilise this tool.

28

29 Key words: rehabilitation; strength, surgery, blood flow restriction.

INTRODUCTION

Light load blood flow restriction (BFR) exercise involves partial restriction of arterial inflow and full restriction of venous outflow from the working muscle during exercise (Scott, Loenneke, Slattery, & Dascombe, 2015). BFR is typically achieved using a pneumatic BFR system, comprised of a cuff connected to an inflation device (Hughes, Rosenblatt, Gissane, Paton, & Patterson, 2018). BFR is commonly applied in combination with light load resistance exercise (RE) using loads corresponding to 20-30% of the individual's one repetition maximum (1RM) (Loenneke, Wilson, Marín, Zourdos, & Bemben, 2012). Light load BFR-RE can stimulate greater increases in skeletal muscle strength and hypertrophy compared to light load RE alone (Loenneke *et al.*, 2012), with some studies reporting adaptations that are similar in magnitude to heavy load RE (Bryk *et al.*, 2016; Kim *et al.*, 2017; Laurentino *et al.*, 2012). A recent meta-analysis demonstrated that light load BFR-RE is equally effective at increasing muscle mass as heavy load RE, and may provide an effective approach for increasing muscle strength in the absence of heavy load RE (Lixandrão *et al.*, 2018). Light load BFR-RE is utilised as a rehabilitation tool in load compromised populations, such as pre-sarcopenic older adults (Libardi *et al.*, 2015), knee osteoarthritis patients (Bryk *et al.*, 2016; Segal, Williams, Davis, Wallace, & Mikesky, 2015; Segal, Davis, & Mikesky, 2015) and anterior cruciate ligament reconstruction (ACLR) patients (Ohta *et al.*, 2003). BFR is reportedly used by practitioners for ACLR rehabilitation in particular (Patterson & Brandner, 2017). One focus of ACLR rehabilitation is attenuating atrophy and regaining muscle mass and strength to restore knee joint stability (Saka, 2014), which typically requires resistance loads of >65% 1RM (Folland & Williams, 2007; Garber *et al.*, 2011). It has been demonstrated that light load BFR-RE is effective for increasing strength in populations with clinical muscle weakness (Hughes, Paton, Rosenblatt, Gissane, & Patterson, 2017), and may be used as an alternative to heavy load RE in the early post-surgery phases of ACLR rehabilitation (Hughes, Rosenblatt, Paton, & Patterson, 2018).

In clinical BFR application patients must be monitored for pain and hypertension (Hughes et al., 2017). Research in non-injured populations demonstrates amplified exercise-induced increases in heart rate, systolic/diastolic blood pressure and mean arterial pressure in light load BFR-RE compared to matched workloads without BFR (Takano *et al.*, 2005; Hollander *et al.*, 2010; Kacin and Strazar, 2011; Vieira *et al.*, 2013; Araújo *et al.*, 2014; Downs *et al.*, 2014). Additionally, perceptual responses to light load RE appear to be augmented with BFR (Loenneke *et al.*, 2011; Loenneke *et al.*, 2012; Staunton *et al.*, 2015). However these responses are not necessarily high; research comparing the cardiovascular and perceptual responses to light load BFR-RE and heavy load RE suggests such responses are similar in magnitude (Brandner, Kidgell, & Warmington, 2015; Hollander et al., 2010; Neto, Santos, et al., 2014; Poton & Polito, 2016). Thus, in non-injured populations light load BFR-RE may provide no greater risk than an equivalent form of exercise at a higher intensity (Jessee et al., 2017).

Much of the research to date comprises heterogeneous protocols and is almost exclusively conducted in non-injured populations. It is unclear if the acute perceptual and blood pressure responses to light load BFR-RE are similar in injured populations, such as ACLR patients, and non-injured populations. It has been hypothesised that the physiological responses to BFR exercise may dictate work volume and patient adherence (Martín-Hernández et al., 2017). Thus, it is important to understand how the acute responses compare to non-injured populations, as this may have implications for decisions regarding application in rehabilitation. Moreover, it is unknown if the acute physiological responses to light load BFR-RE and heavy load RE are similar in ACLR patients, as reported in non-injured populations. If BFR-RE is to be considered as an alternative to heavy load RE for strength rehabilitation in ACLR patients, it is important to examine and compare the acute physiological responses to these exercise modalities, including injury specific aspects such as knee pain (Aglietti, Buzzi, D'Andria, & Zaccherotti, 1993; Shelbourne & Trumper, 1997). Therefore, the aims of this study are to compare the acute physiological responses to 1) light load BFR-RE in non-injured individuals vs. ACLR patients,

55 and 2) light load BFR-RE vs. heavy load RE in ACLR patients. We hypothesised that the acute
56 perceptual response to light load BFR-RE would be 1) higher in ACLR patients compared to non-
57 injured individuals; and 2) similar to HL-RE in ACLR patients, with no differences in post-
58 exercise blood pressure.

METHODOLOGY

Participant information

A total of 30 participants were recruited for this study, which comprised 3 groups: 1) Non-injured individuals performing light load RE with BFR (NI-BFR); 2) ACLR patients performing light load RE with BFR (ACLR-BFR); and 3) ACLR patients performing heavy load RE (ACLR-HL). Participant characteristics for each group are detailed in Table 1. Non-injured participants were active non-smokers free from cardiovascular, pulmonary and metabolic diseases and musculoskeletal injuries in the past 12 months. These aspects also applied to the ACLR patients with the exception that they had undergone ACLR surgery for a unilateral ACL tear. All ACLR surgeries were performed using hamstring autografts (n=20) (Table 1). In the ACLR groups, all participants were assessed to determine they met the criteria required to perform leg press exercise in the early post-surgery phases (weeks 2-3), including minimal swelling, a range of motion of 0-90°, the ability to perform a single leg raise without knee extensor lag and the ability to unilaterally weight bear without pain (Cavanaugh & Powers, 2017). Recent research highlights that early and accelerated post-surgery rehabilitation may improve patient outcomes (Grant, 2013; Tennent et al., 2017), and may begin in the first 2-3 weeks post-surgery when following a criteria-driven approach (Cavanaugh & Powers, 2017; Hughes, Rosenblatt, Paton, et al., 2018). On average, patients in the ACLR-BFR and ACLR-HL groups were 22 ± 2 and 21 ± 3 days post-surgery, respectively, at the time of the familiarisation. Additionally, patients were free from: multiple reconstructive procedures (i.e. multiple ligaments), rheumatoid arthritis, history of deep vein thrombosis or vascular pathology in any lower limb, and the use of anticoagulant medications. All participants refrained from strenuous exercise, caffeine and alcohol in the 24 h prior to testing, and maintained normal dietary habits. All participants provided signed informed consent, in compliance with the Declaration of Helsinki, 7th version, October 2013 (World

Medical Association, 2013). All protocols were approved via the relevant NHS (REC reference: 16/YH/0066) and University ethical committees (SMEC-2015-16-118).

Table 1. Participant group characteristics (Mean \pm SD)

	NI-BFR	ACLR-BFR	ACLR-HL
Number of participants (M/F)	10 (10/0)	10 (6/4)	10 (7/3)
Age (y)	28 \pm 5	29 \pm 5	31 \pm 7
Body mass (kg)	82.6 \pm 13.4	76.5 \pm 15.7	80.7 \pm 12.3
Height (cm)	180.55 \pm 6.83	172.18 \pm 7.67	177.68 \pm 7.57
Body mass index (kg.m ²)	25.25 \pm 3.20	25.69 \pm 4.16	23.51 \pm 3.38
Blood pressure (Systolic/diastolic mmHg)	126 \pm 10/76 \pm 8	125 \pm 3/80 \pm 2	122 \pm 3/81 \pm 4
Mean arterial pressure (mmHg)	93 \pm 5	95 \pm 2	95 \pm 3
Time from surgery to familiarisation (days)	-	22 \pm 2	21 \pm 3
Graft type, <i>n</i>			
Hamstring autograft (%)	-	10 (100%)	10 (100%)

Study design and randomisation

This study was a between-subjects, partially randomised design. At a post-surgery consultant surgeon appointment, ACLR participants were block randomised to either heavy load RE (n=10) or light load BFR-RE (n=10) by an independent member of the research team using 5 x opaque envelopes each with 4 folded slips inside (2 x heavy load RE, 2 x light load BFR-RE).

Experimental procedures

Familiarisation and medical screening

All participants attended a familiarisation session and health screening, followed by one experimental session, separated by a minimum of 48 h. During the familiarisation, body mass and height were recorded to the nearest 0.1 kg and 0.01 cm, respectively; blood pressure was measured in a supine position at the brachial artery; unilateral concentric 10RM was recorded; and participants were familiarised to the RE protocols. Due to the nature of ACLR surgery, 10RM was calculated and used to predict each individual's 1RM (Wathan, 1994) to prescribe RE load for a safer approach to strength testing.

Exercise protocols

All participants performed a warm-up of 5 min of unloaded cycling at a free cadence followed by 10 repetitions of unilateral leg press exercise at a self-selected weight, with a subsequent 5 min rest period. ACLR participants performed the exercise on their injured limb, and non-injured participants on their dominant limb. RE protocols were designed consistent with standard protocols for each type of RE (Fahs, Loenneke, Rossow, Tiebaud, & Bemben, 2012), which is in line with previous studies examining the perceptual and hemodynamic responses to BFR-RE (Brandner & Warmington, 2017; Pinto & Polito, 2016). Participants in the NI-BFR and ACLR-BFR groups then performed 4 sets (30, 15, 15 and 15 repetitions, respectively, with 30 s inter-set rest periods) of unilateral leg press exercise at 30% 1RM throughout 0-90° ROM and a contraction cycle of 1 s concentric/1 s eccentric with BFR applied continuously at 80% limb occlusive pressure (LOP). This set/repetition scheme is common in the BFR literature (Yasuda *et al.*, 2006, 2010, 2012; Loenneke *et al.*, 2012, 2016) and doubling the volume does not appear to augment any adaptations (Loenneke, Fahs, Wilson, & Bemben, 2011; Martín-Hernández *et al.*, 2013). Moreover, completing BFR-RE to volitional failure (Loenneke *et al.*, 2014; Fahs *et al.*, 2015) may not be practical in an early post-surgery setting. The rest period duration of 30 s was selected

as strength gains occur with 30 s inter-set rest periods (Loenneke, Wilson, et al., 2012) and this reflects recommendations for achieving skeletal muscle hypertrophy (Kraemer & Ratamess, 2004). The pressure of 80% LOP was selected based on research suggesting higher pressures maximise fast twitch fibre recruitment and strength adaptations to BFR-RE (Lixandrão et al., 2015; Suga et al., 2012). Participants in the ACLR-HL group performed unilateral leg press exercise (3 x 10 repetitions with 30 s inter-set rest periods) throughout a 0-90° ROM at 70% 1RM, which is a recommended protocol design for improving muscle strength (Garber et al., 2011). Previous research has also suggested that heavy loading following ACLR surgery may not negatively affect knee joint laxity (Bieler et al., 2014) and may be required to increase muscle strength to a satisfactory level (Thomeé et al., 2011).

10RM testing

Participants' isotonic 10RM strength was tested on a spring-loaded leg press (Technogym, Bracknell, UK). Prior to testing participants performed a warm-up of 5 min light cycling followed by 10 repetitions of unilateral leg press at a self-selected weight, separated by 1 min of rest. Concentric 10RM was defined as the maximum load that could be lifted through controlled, full ROM (0-90°) with correct form. Beginning at 80% of predicted 10RM, 10RMs were achieved within 5 attempts, with 3 min of rest between attempts to ensure full muscle recovery (Tobalina, Calleja-González, De Santos, Fernández-López, & Arteaga-Ayarza, 2013).

Blood flow restriction

BFR was achieved using an automatic personalised tourniquet system (PTS) for BFR (Delfi Medical, Vancouver, BC, Canada), comprised of a dual-purpose easy-fit variable contour nylon cuff (11.5 cm x 86 cm, 5 mm thick) connected by airtight hose tubing to a PTS device with LOP calculation sensors and software. The PTS automatically adjusts pressure around the set pressure (McEwen, Jeyasurya, & Owens, 2016) and effectively regulates interface pressure within acceptable limits during BFR-RE (Hughes, Rosenblatt, Gissane, et al., 2018). The Delfi PTS

system automatically calculates LOP by increasing the cuff pressure in stepwise increments, analysing the pneumatic pressure pulsations in the cuff bladder by the arterial pressure pulsations at each cuff pressure increment, and uses these characteristics to determine LOP (McEwen, Masri, Day, & Younger, 2015). Previous research demonstrates that measurement of lower limb LOP with this system concurs with the gold standard doppler technique of calculating LOP (McEwen et al., 2015). LOP was calculated with the participants in the position for exercise to ensure accurate calculation of LOP (Hughes, Jeffries, Waldron, et al., 2018).

Perceptual responses

Perceptual responses were assessed following each set using Borg's ratings of perceived exertion (RPE) and pain (RPP) scales (Borg & Löllgen, 1998). Participants received verbal instructions on rating both during the familiarisation visit and were reminded at the experimental session. The pain scale ranges from 0 to 11; for muscle pain, participants were instructed that 10 was their reference point representing their previous worst felt pain, and a score of 11 represented worse pain than any they had ever felt before, similar to previous research examining discomfort during BFR (Dankel et al., 2017; Jessee et al., 2017). This same explanation was used to instruct patients on how to rate knee pain. Muscle pain was assessed in all 3 groups. Participants in the ACLR-BFR and ACLR-HL groups were also asked to provide a score for knee pain; participants were instructed that this score represented any pain felt within the knee joint capsule. ACLR participants were also contacted 24 hr post-exercise to provide a knee pain score. Knee pain was not assessed in the NI-BFR group as any knee pain during the familiarisation session likely indicated a musculoskeletal problem that was grounds for exclusion from the study. For RPE, participants were instructed that a rating of 6 meant they felt no exertion, and 20 meant they were giving maximal effort and could not exert themselves any further (Dankel et al., 2017). For both pain and RPE the final exercising values were used for analysis to provide session ratings, which is line with previous studies (Brandner & Warmington, 2017; Neto, Sousa, et al., 2014; Vieira et al., 2014).

Blood pressure

Systolic and diastolic blood pressure (mmHg) was measured at the brachial artery at pre-exercise and 5 min post-exercise using a Mobil-O-Graph ambulatory blood pressure monitor connected to a laptop with Hypertension Management software (IEM, Cockerillstrasse, Stolberg, Germany). This system measures peripheral blood pressure and records the systolic and diastolic data.

Statistical analysis

All data was stored on the password protected servers at the NHS hospital and university. All data were analysed using IBM SPSS Statistics Version 24.0 (IBM Corp, Chicago IL, United States of America). Data are presented as mean \pm standard deviation with 95% confidence intervals (CIs) unless otherwise stated. Normal distribution of data was assessed using Shapiro-Wilks test ($p>0.05$), and homogeneity of variances (where appropriate) was assessed using Levene's Test of Homogeneity of variances ($p>0.05$). Pearson's r correlation test was used to examine any relationship between total exercise volume and each perceptual measure. Final RPE and muscle pain scores were assessed using one-way between subjects' ANOVAs. Data for 24 h post-exercise knee pain was non-normally distributed; a logarithmic transformation was applied and the normally distributed ($p>0.05$) data for knee pain was assessed using a two-way between subjects' ANOVA. LOP, 1RM, exercise load and volume were assessed using independent samples' t -tests. Blood pressure was assessed using one-way between subject's ANOVAs. For any statistically significant interaction determined by ANOVA, Bonferroni post-hoc analysis was performed to examine the differences. Alpha significance was set *a priori* $p<0.05$.

RESULTS

Participants

All 30 participants completed the study with no adverse events. Correlation analysis found no significant relationship between total exercise volume and perceptual measures. Mean \pm SD for RE loads, volume and BFR pressures are detailed in Table 2.

Table 2. Exercise load, volume and BFR pressures (mean \pm SD).

	NI-BFR	ACLR-BFR	ACLR heavy
1RM (kg)	161 \pm 44	61 \pm 28*	57 \pm 17*
Exercise load (kg)	48 \pm 13	16 \pm 9*	38 \pm 11*
Exercise volume (Reps)	75 \pm 0	64 \pm 13*	30 \pm 0**
LOP (mmHg)	173 \pm 22	186 \pm 28	-
80% LOP (mmHg)	138 \pm 18	148 \pm 22	-

*=significantly lower than NI-BFR group ($p < 0.05$); †=significantly lower than ACLR-BFR group ($p < 0.05$)

RPE

RPE was statistically significantly different between the groups, $F_{(2, 27)} = 6.098$, $p < 0.01$. RPE was higher in the ACLR-BFR group compared to the NI-BFR group, a mean difference of 3.4 ± 1 (95% CI: 0.825 to 5.975, $p < 0.01$). There were no differences in RPE between the ACLR-BFR group and the ACLR-HL (mean difference of 2.5 ± 1 , 95% CI: -0.075 to 5.075, $p > 0.05$). There were no differences in RPE between the ACLR-HL and NI-BFR groups (mean difference of 0.9 ± 1 (95% CI: -1.675 to 3.475, $p > 0.05$) (Figure 1).

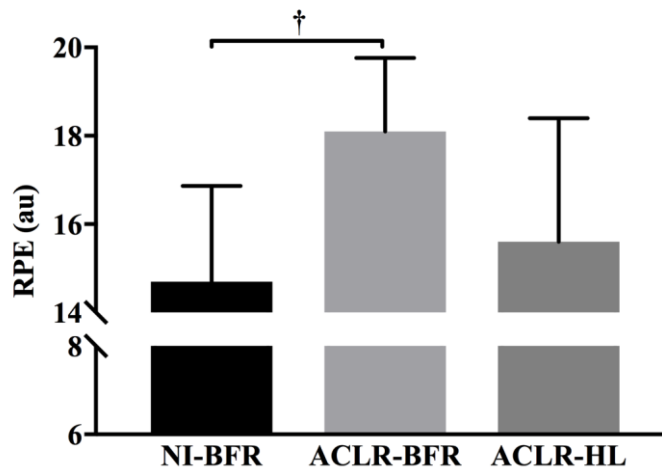


Figure 1. Session rating of perceived exertion in the three groups (mean \pm SD). † indicates a significant difference ($p<0.01$).

Muscle pain

Muscle pain was statistically significantly different between the groups, $F_{(2, 27)} = 16.084$, $p<0.01$. Muscle pain was higher in the ACLR-BFR group compared to the NI-BFR group, a mean difference of 2.7 ± 1 (95% CI: 0.292 to 5.058, $p<0.05$). Muscle pain was higher in the ACLR-BFR group compared to the ACLR-HL group, a mean difference of 5 ± 1 (95% CI: 2.942 to 7.758, $p<0.01$). Muscle pain was higher in the NI-BFR group compared to the ACLR-HL group, a mean difference of 3 ± 1 (95% CI: 0.242 to 5.058, $p<0.05$) (Figure 2).

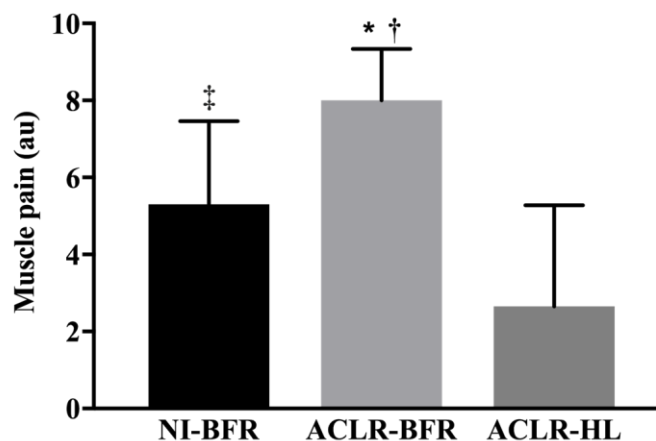


Figure 2. Session rating of muscle pain in the 3 groups (mean \pm SD). * indicates a significant difference compared to NI-BR group ($p<0.05$); † indicates a significant difference compared to ACLR-HL group ($p<0.01$); ‡ indicates a significant difference compared to ACLR-HL group ($p<0.05$)

Knee pain

There was no statistically significant interaction between the groups and timepoints for knee pain, $F_{(1, 36)} = 0.123$, $p > 0.05$. A main effect of treatment on knee pain was found, $F_{(1, 38)} = 21.992$, $p < 0.001$. Knee pain was lower in the ACLR-BFR group compared to the ACLR-HL group, a mean difference of 1.3 (95% CI: -1.890 to -0.750, $p < 0.01$) (Figure 3 and Figure 4).

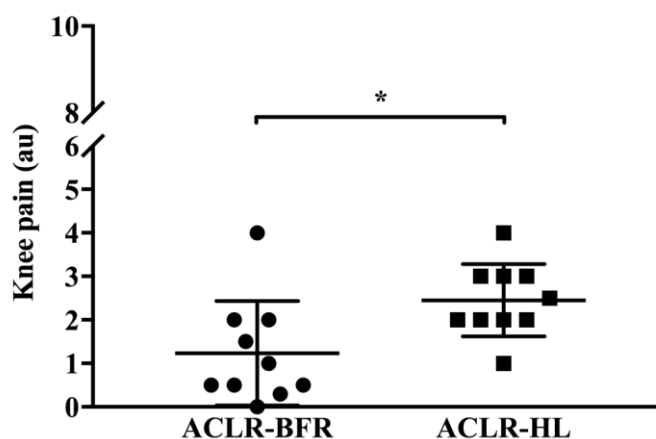


Figure 3. Session knee pain score in the ACLR groups (mean \pm SD). * indicates a significant difference ($p < 0.05$).

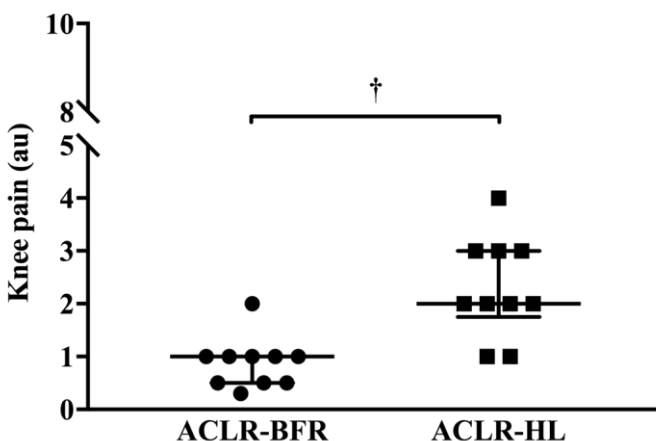


Figure 4. 24 hr post-exercise knee pain scores in the ACLR-BFR and ACLR-HL groups (median \pm IQR). † indicates a significant difference ($p < 0.01$).

Blood pressure

There were no differences in pre- and post-exercise blood pressure between any groups (Table 3).

Table 3. Pre- and 5 min post-exercise blood pressure in each group (mean \pm SD).

	Pre-exercise blood pressure (mmHg)		Post-exercise blood pressure (mmHg)	
	<i>Systolic</i>	<i>Diastolic</i>	<i>Systolic</i>	<i>Diastolic</i>
NI-BFR	127 \pm 10	80 \pm 3	129 \pm 13	78 \pm 5
ACLR-BFR	130 \pm 9	78 \pm 6	131 \pm 12	82 \pm 7
ACLR-HL	139 \pm 9	85 \pm 4	139 \pm 9	82 \pm 4

DISCUSSION

This study was the first to compare the acute perceptual and hemodynamic responses to heavy load RE and light load BFR-RE in clinical populations. The main findings were: 1) RPE was higher in the ACLR-BFR group compared to the non-injured BFR group, but similar to the ACLR-HL group; 2) Muscle pain was higher in both BFR groups compared to the ACLR-HL group; 3) Session knee pain and 24 hr post-exercise knee pain was lower in the ACLR-BFR group compared to the ACLR-HL group; and 4) There were no differences in pre- and post-exercise blood pressure between the groups.

Research in non-injured populations suggests the perceptual responses to light load BFR-RE are similar to, or greater than, heavy load RE (Brandner & Warmington, 2017; Hollander et al., 2010; Loenneke et al., 2015; Vieira et al., 2014). In a randomised crossover design, Hollander et al. (2010) demonstrated comparable increases in RPE response to an acute bout of light load BFR-RE (30% 1RM) and heavy load RE (70% 1RM) in non-injured populations, which is in line with the findings of Loenneke *et al.* (2015). The present study demonstrates similar findings, suggesting that the acute RPE response to light load BFR-RE is not greater than heavy load RE in ACLR patients. It has been demonstrated that proximal arterial occlusion of a limb during exercise results in overestimation of perceived force (Takarada, Nozaki, & Taira, 2006), which may explain the findings of the present study and previous research. Although the mechanisms of increased estimation of effort with light loads and BFR are not fully understood, it has been proposed that impeded conduction in peripheral nerves due to mechanical deformation during compression and inhibition of cutaneous sensory nerves may alter the response of somatic efferent neurons (Hollander et al., 2010; Takarada et al., 2006). Additionally, post-surgery volitional muscle activation failure (Perraton et al., 2017) caused by failure of the central nervous system to activate the knee extensor muscles (Mizner, Petterson, Stevens, Vandenborne, & Snyder-

Mackler, 2005) may contribute to a greater RPE response in the ACLR-BFR group compared to the non-injured BFR group at the same relative exercise load.

In the present study, muscle pain scores were higher in both the non-injured BFR and ACLR-BFR groups compared to the ACLR-HL group. There is an increase in pain perception with light load BFR exercise alongside increased muscle activation (Wernbom, Järrebring, Andreasson, & Augustsson, 2009) which has been attributed to metabolite accumulation due to venous occlusion and hypoxia (Suga et al., 2009). It is hypothesised that this may stimulate group III and IV afferent fibres, increasing sympathetic nervous system activity (Takarada et al., 2000). The observation of higher pain scores in the present study is in contrast to previous work demonstrating similar perceptions of pain between light load BFR-RE (30% 1RM) and heavy load (70% 1RM) exercise (Hollander et al., 2010). However, the restriction pressures used in the present study (173 and 186 mmHg for the NI-BFR and ACLR-BFR groups, respectively) were likely higher than those used by Hollander et al. (20% below systolic blood pressure). Higher pressures may cause greater accumulation of metabolites (Yasuda, Abe, et al., 2010), which may increase perception of discomfort (Jessee et al., 2017). Moreover, in the present study a greater total volume of work was completed by the BFR groups, which may have influenced pain responses due to greater time under BFR. Regarding the BFR groups only, muscle pain and strains that are observed following ACLR surgery (D'Alessandro, Wake, & Annear, 2013) may contribute to the higher pain scores observed in the ACLR-BFR group compared to the non-injured BFR group, particularly if the ACLR-BFR group were present with some degree of muscle pain prior to exercise.

Knee pain is widely reported following ACLR surgery, particularly in the anterior knee compartment (Chmielewski et al., 2008), and may predict a more difficult and prolonged rehabilitation process (Dunn et al., 2010). Knee pain has been linked to concomitant injuries such as bone bruising and cartilage/meniscal damage (Hughes, Rosenblatt, Paton, et al., 2018), and pain intensity is associated with self-reported function following surgery and successful return to

sport (Chmielewski et al., 2008; Czappon, Racette, Klein, & Harris-Hayes, 2014). Thus, minimising knee pain in early strength rehabilitation is important. In the present study, the ACLR-BFR group experienced less knee pain during RE, likely due to the lower loads (30% vs. 70% 1RM) and lower knee joint forces during RE. Interestingly, the ACLR-BFR group also reported less knee pain in the 24 hours following exercise. This suggests light load BFR-RE in the early post-surgery phases may not exacerbate pain or inflammation within the knee joint on subsequent days after training, which may positively influence exercise volume during sessions and patient adherence to a rehabilitation programme (Juan Martín-Hernández et al., 2017). Therefore, similarly to research in non-injured populations, light load BFR-RE may be used more frequently than heavy load RE, such as twice daily (Abe, Kawamoto, *et al.*, 2005; Yasuda, Fujita, *et al.*, 2010). Adaptations in muscle strength and mass have been observed in short time frames such as two weeks (Abe, Yasuda, et al., 2005; Yasuda et al., 2005) and even one week (Abe, Kawamoto, et al., 2005; Fujita, Brechue, Kurita, Sato, & Abe, 2008), thus the findings of the present study may have important implications for the use of BFR in early ACLR rehabilitation.

Collectively, the findings of the present study suggest that the perceptual responses to light load BFR-RE are similar or greater than heavy load RE in ACLR patients. Previous research suggests that exacerbated perceptual responses subside after a few exercise sessions with BFR (Clarkson, Conway, & Warmington, 2017; Fitschen et al., 2014; Weatherholt, Beekley, Greer, Urtel, & Mikesky, 2013), suggesting an adaptive effect facilitating tolerance with exposure (Brandner et al., 2018). Moreover, there appears to be a similar time course of adaptation to perceptual responses between light load BFR-RE and heavy load RE (Juan Martín-Hernández et al., 2017). Although it is unknown if the time course of adaptation in ACLR populations is similar, collectively these reports and the findings of the present study suggest that high initial perceptual responses may not be a limiting factor when using BFR in an ACLR rehabilitation programme (Loenneke et al., 2016).

Finally, the present study found no differences in post-exercise blood pressure between the groups. This is in line with previous research demonstrating similar blood pressure responses in light load BFR-RE and heavy load RE (Brandner et al., 2015; Neto, Santos, et al., 2014; Poton & Polito, 2016; Sardeli et al., 2017). Thus, light load BFR-RE likely provides no greater hemodynamic risk than heavy load RE (Jessee et al., 2017). Moreover, these findings are in line with previous work indicating return to baseline of mean arterial pressure following BFR-RE with the Delfi PTS device (Hughes, Rosenblatt, Gissane, et al., 2018). However, it is of note that the blood pressure response to unilateral exercise is likely lower than bilateral exercise with greater muscle mass involvement (Adams, Cline, Hubbard, McCullough, & Hartman, 2006), therefore the findings of the present study may be specific to unilateral exercise only.

There are several limitations to this study. Firstly, total exercise volume was heterogeneous between groups, therefore a volume effect on perceptual responses cannot be disregarded; however, the protocols used reflect current guidelines for light load BFR-RE and heavy load RE for improving muscle strength and mass. Secondly, we could not quantify overall presence or severity of any concomitant pathologies, which may also impact upon the perceptual responses to RE; however, post-surgery pathologies vary in incidence and severity in ACLR patients and thus are difficult to account for (Tahami & Rad, 2015). Thirdly, our NI-BFR group was composed of males only. Literature suggests that the perceptual response to relative RE load is similar between males and females (Pincivero, Coelho, & Campy, 2003), however at present there is a lack of research concerning gender differences in the perceptual response to BFR exercise which may impact the findings of the present study. Finally, the findings of the present study may be specific to the RE protocols used.

CONCLUSION

Collectively, the findings of present study suggest that the hemodynamic and perceptual responses to light load BFR-RE in ACLR patients may not be a limiting factor for clinician concern in a rehabilitation setting, and that this mode of exercise may favourably influence knee pain during and throughout a training programme. Future research should monitor these responses over the course of a rehabilitation training programme.

References

- Abe, T., Kawamoto, K., Yasuda, T., Kearns, C. F., Midorikawa, T., & Sato, Y. (2005). Eight days KAATSU-resistance training improved sprint but not jump performance in collegiate male track and field athletes. *International Journal of KAATSU Training Research*, 1(1), 19–23. <https://doi.org/10.3806/ijktr.1.19>
- Abe, T., Yasuda, T., Midorikawa, T., Sato, Y., Kearns, C. F., Inoue, K., ... Ishii, N. (2005). Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily “KAATSU” resistance training. *International Journal of KAATSU Training Research*, 1(1), 6–12. <https://doi.org/10.3806/ijktr.1.6>
- Adams, J., Cline, M. J., Hubbard, M., McCullough, T., & Hartman, J. (2006). A new paradigm for post-cardiac event resistance exercise guidelines. *American Journal of Cardiology*, 97(2), 281–286. <https://doi.org/10.1016/j.amjcard.2005.08.035>
- Aglietti, P., Buzzi, R., D’Andria, S., & Zaccherotti, G. (1993). Patellofemoral problems after intraarticular anterior cruciate ligament reconstruction. *Clinical Orthopaedics and Related Research*, 17(6), 195–204. <https://doi.org/10.1097/00003086-199303000-00025>
- Araújo, J. P., Silva, E. D., Silva, J. C. G., Souza, T. S. P., Lima, E. O., Guerra, I., & Sousa, M. S. C. (2014). The acute effect of resistance exercise with blood flow restriction with hemodynamic variables on hypertensive subjects. *Journal of Human Kinetics*, 43(1), 79–85. <https://doi.org/10.2478/hukin-2014-0092>
- Bieler, T., Aue Sobol, N., Andersen, L. L., Kiel, P., Løfholm, P., Aagaard, P., ... Beyer, N. (2014). The effects of high-intensity versus low-intensity resistance training on leg extensor power and recovery of knee function after ACL-reconstruction. *BioMed Research International*, 2014. <https://doi.org/10.1155/2014/278512>
- Borg, G., & Löllgen, H. (1998). *Borg’s perceived exertion and pain scales*. *Deutsche Zeitschrift für Sportmedizin* (Vol. 52). Human Kinetics. <https://doi.org/10.1097/00005768-199809000-00018>
- Brandner, C. R., Kidgell, D. J., & Warmington, S. A. (2015). Unilateral bicep curl hemodynamics: Low-pressure continuous vs high-pressure intermittent blood flow restriction. *Scandinavian Journal of Medicine and Science in Sports*, 25(6), 770–777. <https://doi.org/10.1111/sms.12297>
- Brandner, C. R., May, A. K., Clarkson, M. J., & Warmington, S. A. (2018). Reported Side-effects and Safety Considerations for the Use of Blood Flow Restriction During Exercise in Practice and Research. *Techniques in Orthopaedics*, 00(00), 1. <https://doi.org/10.1097/BTO.0000000000000259>
- Brandner, C. R., & Warmington, S. A. (2017). Delayed onset muscle soreness and perceived exertion after blood flow restriction exercise. *Journal of Strength and Conditioning Research*, 31(11), 3101–3108. <https://doi.org/10.1519/JSC.0000000000001779>
- Bryk, F. F., dos Reis, A. C., Fingerhut, D., Araujo, T., Schutzer, M., Cury, R. de P. L., ... Fukuda, T. Y. (2016).

- Exercises with partial vascular occlusion in patients with knee osteoarthritis: a randomized clinical trial. *Knee Surgery, Sports Traumatology, Arthroscopy*, 24(5), 1580–1586. <https://doi.org/10.1007/s00167-016-4064-7>
- Cavanaugh, J. T., & Powers, M. (2017). ACL Rehabilitation Progression: Where Are We Now? *Current Reviews in Musculoskeletal Medicine*, 10(3), 289–296. <https://doi.org/10.1007/s12178-017-9426-3>
- Chmielewski, T. L., Jones, D., Day, T., Tillman, S. M., Lentz, T. A., & George, S. Z. (2008). The Association of Pain and Fear of Movement/Reinjury With Function During Anterior Cruciate Ligament Reconstruction Rehabilitation. *Journal of Orthopaedic & Sports Physical Therapy*, 38(12), 746–753. <https://doi.org/10.2519/jospt.2008.2887>
- Clarkson, M. J., Conway, L., & Warmington, S. A. (2017). Blood flow restriction walking and physical function in older adults: A randomized control trial. *Journal of Science and Medicine in Sport*, 20(12), 1041–1046. <https://doi.org/10.1016/j.jsams.2017.04.012>
- Cook, S. B., Clark, B. C., & Ploutz-Snyder, L. L. (2007). Effects of exercise load and blood-flow restriction on skeletal muscle function. *Medicine and Science in Sports and Exercise*, 39(10), 1708–1713. <https://doi.org/10.1249/mss.0b013e31812383d6>
- Cook, S. B., Murphy, B. G., & Labarbera, K. E. (2013). Neuromuscular function after a bout of low-load blood flow-restricted exercise. *Medicine and Science in Sports and Exercise*, 45(1), 67–74. <https://doi.org/10.1249/MSS.0b013e31826c6fa8>
- Czuppon, S., Racette, B. A., Klein, S. E., & Harris-Hayes, M. (2014). Variables associated with return to sport following anterior cruciate ligament reconstruction: A systematic review. *British Journal of Sports Medicine*, 48(5), 356–364. <https://doi.org/10.1136/bjsports-2012-091786>
- D'Alessandro, P., Wake, G., & Annear, P. (2013). Hamstring pain and muscle strains following anterior cruciate ligament reconstruction: a prospective, randomized trial comparing hamstring graft harvest techniques. *The Journal of Knee Surgery*, 26(2), 139–144. <https://doi.org/10.1055/s-0032-1324811>
- Dankel, S., Buckner, S., Counts, B., Jessee, M., Mouser, J., Mattocks, K., ... Loenneke, J. (2017). The acute muscular response to two distinct blood flow restriction protocols. *Physiology International*, 104(1), 64–76. <https://doi.org/10.1556/2060.104.2017.1.1>
- Downs, M. E., Hackney, K. J., Martin, D., Caine, T. L., Cunningham, D., O'Connor, D. P., & Ploutz-Snyder, L. L. (2014). Acute vascular and cardiovascular responses to blood flow-restricted exercise. *Medicine and Science in Sports and Exercise*, 46(8), 1489–1497. <https://doi.org/10.1249/MSS.0000000000000253>
- Dunn, W. R., Spindler, K. P., Amendola, A., Andrich, J. T., Kaeding, C. C., Marx, R. G., ... Wolf, B. R. (2010). Which preoperative factors, including bone bruise, are associated with knee pain/ symptoms at index anterior cruciate ligament reconstruction (ACLR)?: A multicenter orthopaedic outcomes network (MOON) aclr cohort

- study. *American Journal of Sports Medicine*, 38(9), 1778–1787. <https://doi.org/10.1177/0363546510370279>
- Fahs, C. A., Loenneke, J. P., Rossow, L. M., Tiebaud, R. S., & Bembien, M. G. (2012). Methodological considerations for blood flow restricted resistance exercise. *Journal of Trainology*, 1(1), 14–22. https://doi.org/10.17338/trainology.1.1_14
- Fahs, C. A., Loenneke, J. P., Thiebaud, R. S., Rossow, L. M., Kim, D., Abe, T., ... Bembien, M. G. (2015). Muscular adaptations to fatiguing exercise with and without blood flow restriction. *Clinical Physiology and Functional Imaging*, 35(3), 167–176. <https://doi.org/10.1111/cpf.12141>
- Fitschen, P. J., Kistler, B. M., Jeong, J. H., Chung, H. R., Wu, P. T., Walsh, M. J., & Wilund, K. R. (2014). Perceptual effects and efficacy of intermittent or continuous blood flow restriction resistance training. *Clinical Physiology and Functional Imaging*, 34(5), 356–363. <https://doi.org/10.1111/cpf.12100>
- Folland, J. P., & Williams, A. G. (2007). The adaptations to strength training: Morphological and neurological contributions to increased strength. *Sports Medicine*, 37(2), 145–168. <https://doi.org/10.2165/00007256-200737020-00004>
- Fujita, T., Brechue, W. F., Kurita, K., Sato, Y., & Abe, T. (2008). Increased muscle volume and strength following six days of low-intensity resistance training with restricted muscle blood flow. *International Journal of KAATSU Training Research*, 4(1), 1–8. <https://doi.org/10.3806/ijktr.4.1>
- Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., ... Swain, D. P. (2011). Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Medicine and Science in Sports and Exercise*, 43(7), 1334–1359. <https://doi.org/10.1249/MSS.0b013e318213febf>
- Grant, J. A. (2013). Updating Recommendations for Rehabilitation after ACL Reconstruction: a Review. *Clinical Journal of Sport Medicine : Official Journal of the Canadian Academy of Sport Medicine*, 23(6), 501–502. <https://doi.org/10.1097/JSM.0000000000000044>
- Hollander, D. B., Reeves, G. V., Clavier, J. D., Francois, M. R., Thomas, C., & Kraemer, R. R. (2010). Partial occlusion during resistance exercise alters effort sense and pain. *Journal of Strength and Conditioning Research*, 24(1), 235–243. <https://doi.org/10.1519/JSC.0b013e3181c7badf>
- Hughes, L., Jeffries, O., Waldron, M., Rosenblatt, B., Gissane, C., Paton, B., & Patterson, S. D. (2018). Influence and reliability of lower-limb arterial occlusion pressure at different body positions. *PeerJ*, 2018(5), In press. <https://doi.org/10.1074/jbc.M115.641514>
- Hughes, L., Paton, B., Rosenblatt, B., Gissane, C., & Patterson, S. D. (2017). Blood flow restriction training in clinical musculoskeletal rehabilitation: A systematic review and meta-analysis. *British Journal of Sports Medicine*, 51(13), 1003–1011. <https://doi.org/10.1136/bjsports-2016-097071>

- Hughes, L., Rosenblatt, B., Gissane, C., Paton, B., & Patterson, S. D. (2018). Interface pressure, perceptual and mean arterial pressure responses to different blood flow restriction systems. *Scandinavian Journal of Medicine & Science in Sports*, (March), 1–9. <https://doi.org/10.1111/sms.13092>
- Hughes, L., Rosenblatt, B., Paton, B., & Patterson, S. D. (2018). Blood Flow Restriction Training in Rehabilitation Following Anterior Cruciate Ligament Reconstructive Surgery : A Review. *Techniques in Orthopaedics*, 00(00), 1–9.
- Jessee, M. B., Dankel, S. J., Buckner, S. L., Mouser, J. G., Mattocks, K. T., & Loenneke, J. P. (2017). The Cardiovascular and Perceptual Response to Very Low Load Blood Flow Restricted Exercise Authors. *International Journal of Sports Medicine*, 38(8), 597–603. <https://doi.org/10.1055/s-0043-109555>
- Kacin, A., & Strazar, K. (2011). Frequent low-load ischemic resistance exercise to failure enhances muscle oxygen delivery and endurance capacity. *Scandinavian Journal of Medicine and Science in Sports*, 21(6), 231–241. <https://doi.org/10.1111/j.1600-0838.2010.01260.x>
- Kim, D., Loenneke, J. P., Ye, X., Bemben, D. A., Beck, T. W., Larson, R. D., & Bemben, M. G. (2017). Low-load resistance training with low relative pressure produces muscular changes similar to high-load resistance training. *Muscle and Nerve*, 56(6), E126–E133. <https://doi.org/10.1002/mus.25626>
- Kraemer, W. J., & Ratamess, N. A. (2004). Fundamentals of Resistance Training: Progression and Exercise Prescription. *Medicine and Science in Sports and Exercise*, 36(4), 674–688. <https://doi.org/10.1249/01.MSS.0000121945.36635.61>
- Laurentino, G. C., Ugrinowitsch, C., Roschel, H., Aoki, M. S., Soares, A. G., Neves, M., ... Tricoli, V. (2012). Strength training with blood flow restriction diminishes myostatin gene expression. *Medicine and Science in Sports and Exercise*, 44(3), 406–412. <https://doi.org/10.1249/MSS.0b013e318233b4bc>
- Libardi, C., Chacon-Mikahil, M., Cavaglieri, C., Tricoli, V., Roschel, H., Vechin, F., ... Ugrinowitsch, C. (2015). Effect of Concurrent Training with Blood Flow Restriction in the Elderly. *International Journal of Sports Medicine*, 36(05), 395–399. <https://doi.org/10.1055/s-0034-1390496>
- Lixandrão, M. E., Ugrinowitsch, C., Berton, R., Vechin, F. C., Conceição, M. S., Damas, F., ... Roschel, H. (2018). Magnitude of Muscle Strength and Mass Adaptations Between High-Load Resistance Training Versus Low-Load Resistance Training Associated with Blood-Flow Restriction: A Systematic Review and Meta-Analysis. *Sports Medicine*, 48(2), 361–378. <https://doi.org/10.1007/s40279-017-0795-y>
- Lixandrão, M. E., Ugrinowitsch, C., Laurentino, G., Libardi, C. A., Aihara, A. Y., Cardoso, F. N., ... Roschel, H. (2015). Effects of exercise intensity and occlusion pressure after 12 weeks of resistance training with blood-flow restriction. *European Journal of Applied Physiology*, 115(12), 2471–2480. <https://doi.org/10.1007/s00421-015-3253-2>

- Loenneke, J. P., Balapur, A., Thrower, A. D., Barnes, J., & Pujol, T. J. (2012). Blood flow restriction reduces time to muscular failure. *European Journal of Sport Science*, 12(3), 238–243.
<https://doi.org/10.1080/17461391.2010.551420>
- Loenneke, J. P., Balapur, A., Thrower, A. D., Barnes, J. T., & Pujol, T. J. (2011). The perceptual responses to occluded exercise. *International Journal of Sports Medicine*, 32(3), 181–184. <https://doi.org/10.1055/s-0030-1268472>
- Loenneke, J. P., Fahs, C. A., Wilson, J. M., & Bembien, M. G. (2011). Blood flow restriction: The metabolite/volume threshold theory. *Medical Hypotheses*, 77(5), 748–752. <https://doi.org/10.1016/j.mehy.2011.07.029>
- Loenneke, J. P., Kim, D., Fahs, C. A., Thiebaud, R. S., Abe, T., Larson, R. D., ... Bembien, M. G. (2015). The effects of resistance exercise with and without different degrees of blood-flow restriction on perceptual responses. *Journal of Sports Sciences*, 33(14), 1472–1479. <https://doi.org/10.1080/02640414.2014.992036>
- Loenneke, J. P., Kim, D., Fahs, C. A., Thiebaud, R. S., Abe, T., Larson, R. D., ... Bembien, M. G. (2017). The influence of exercise load with and without different levels of blood flow restriction on acute changes in muscle thickness and lactate. *Clinical Physiology and Functional Imaging*, 37(6), 734–740.
<https://doi.org/10.1111/cpf.12367>
- Loenneke, J. P., Kim, D., Mouser, J. G., Allen, K. M., Thiebaud, R. S., Abe, T., & Bembien, M. G. (2016). Are there perceptual differences to varying levels of blood flow restriction? *Physiology and Behavior*, 157, 277–280.
<https://doi.org/10.1016/j.physbeh.2016.02.022>
- Loenneke, J. P., Thiebaud, R. S., Fahs, C. A., Rossow, L. M., Abe, T., & Bembien, M. G. (2014). Blood flow restriction: Effects of cuff type on fatigue and perceptual responses to resistance exercise. *Acta Physiologica Hungarica*, 101(2), 158–166. <https://doi.org/10.1556/APhysiol.101.2014.2.4>
- Loenneke, J. P., Wilson, J. M., Marín, P. J., Zourdos, M. C., & Bembien, M. G. (2012). Low intensity blood flow restriction training: A meta-analysis. *European Journal of Applied Physiology*, 112(5), 1849–1859.
<https://doi.org/10.1007/s00421-011-2167-x>
- Madarame, H., Neya, M., Ochi, E., Nakazato, K., Sato, Y., & Ishii, N. (2008). Cross-transfer effects of resistance training with blood flow restriction. *Medicine and Science in Sports and Exercise*, 40(2), 258–263.
<https://doi.org/10.1249/mss.0b013e31815c6d7e>
- Manini, T. M., Yarrow, J. F., Buford, T. W., Clark, B. C., Conover, C. F., & Borst, S. E. (2012). Growth hormone responses to acute resistance exercise with vascular restriction in young and old men. *Growth Hormone and IGF Research*, 22(5), 167–172. <https://doi.org/10.1016/j.ghir.2012.05.002>
- Martín-Hernández, J., Marín, P. J., Menéndez, H., Ferrero, C., Loenneke, J. P., & Herrero, A. J. (2013). Muscular adaptations after two different volumes of blood flow-restricted training. *Scandinavian Journal of Medicine*

- and *Science in Sports*, 23(2), 1–7. <https://doi.org/10.1111/sms.12036>
- Martín-Hernández, J., Ruiz-Aguado, J., Herrero, A. J., Loenneke, J. P., Aagaard, P., Cristi-Montero, C., ... Marín, P. J. (2017). Adaptation of Perceptual Responses to Low-Load Blood Flow Restriction Training. *Journal of Strength and Conditioning Research*, 31(3), 765–772. <https://doi.org/10.1519/JSC.0000000000001478>
- May, A. K., Brandner, C. R., & Warmington, S. A. (2017). Hemodynamic responses are reduced with aerobic compared with resistance blood flow restriction exercise. *Physiological Reports*, 5(3), e13142. <https://doi.org/10.14814/phy2.13142>
- McEwen, J. A., Jeyasurya, J., & Owens, J. (2016). How can personalised tourniquet systems accelerate rehabilitation of wounded warriors, professional athletes and orthopaedic patients? *39th of The Canadian Medical and Biological Engineering Conference*.
- McEwen, J. A., Masri, B. A., Day, B., & Younger, A. S. (2015). World congress on medical physics and biomedical engineering, june 7-12, 2015, Toronto, Canada. *IFMBE Proceedings*, 51(November 2016). <https://doi.org/10.1007/978-3-319-19387-8>
- Mizner, R. L., Petterson, S. C., Stevens, J. E., Vandenborne, K., & Snyder-Mackler, L. (2005). Early quadriceps strength loss after total knee arthroplasty: The contributions of muscle atrophy and failure of voluntary muscle activation. *Journal of Bone and Joint Surgery - Series A*, 87(5), 1047–1053. <https://doi.org/10.2106/JBJS.D.01992>
- Neto, G. R., Santos, H. H., Sousa, J. B. C., Júnior, A. T. A., Araújo, J. P., Aniceto, R. R., & Sousa, M. S. C. (2014). Effects of High-Intensity Blood Flow Restriction Exercise on Muscle Fatigue. *Journal of Human Kinetics*, 41(1), 163–172. <https://doi.org/10.2478/hukin-2014-0044>
- Neto, G. R., Sousa, M. S. C., Costa e Silva, G. V., Gil, A. L. S., Salles, B. F., & Novaes, J. S. (2014). Acute resistance exercise with blood flow restriction effects on heart rate, double product, oxygen saturation and perceived exertion. *Clinical Physiology and Functional Imaging*, 36(1), 53–59. <https://doi.org/10.1111/cpf.12193>
- Nielsen, J. L., Aagaard, P., Bech, R. D., Nygaard, T., Hvid, L. G., Wernbom, M., ... Frandsen, U. (2012). Proliferation of myogenic stem cells in human skeletal muscle in response to low-load resistance training with blood flow restriction. *Journal of Physiology*, 590(17), 4351–4361. <https://doi.org/10.1113/jphysiol.2012.237008>
- Ogasawara, R., Loenneke, J. P., Thiebaud, R. S., & Abe, T. (2013). Low-Load Bench Press Training to Fatigue Results in Muscle Hypertrophy Similar to High-Load Bench Press Training. *International Journal of Clinical Medicine*, 04(02), 114–121. <https://doi.org/10.4236/ijcm.2013.42022>
- Ohta, H., Kurosawa, H., Ikeda, H., Iwase, Y., Satou, N., & Nakamura, S. (2003). Low-load resistance muscular

- training with moderate restriction of blood flow after anterior cruciate ligament reconstruction. *Acta Orthopaedica Scandinavica*, 74(1), 62–68. <https://doi.org/10.1080/00016470310013680>
- Ozaki, H., Yasuda, T., Ogasawara, R., Sakamaki-Sunaga, M., Naito, H., & Abe, T. (2013). Effects of high-intensity and blood flow-restricted low-intensity resistance training on carotid arterial compliance: Role of blood pressure during training sessions. *European Journal of Applied Physiology*, 113(1), 167–174. <https://doi.org/10.1007/s00421-012-2422-9>
- Patterson, S. D., & Brandner, C. R. (2017). The role of blood flow restriction training for applied practitioners: A questionnaire-based survey. *Journal of Sports Sciences*, 36(2), 123–130. <https://doi.org/10.1080/02640414.2017.1284341>
- Patterson, S. D., Hughes, L., Head, P., Warmington, S., & Brandner, C. (2017). Blood flow restriction training: A novel approach to augment clinical rehabilitation: How to do it. *British Journal of Sports Medicine*, 51(23), 1648–1649. <https://doi.org/10.1136/bjsports-2017-097738>
- Perraton, L., Clark, R., Crossley, K., Pua, Y.-H., Whitehead, T., Morris, H., ... Bryant, A. (2017). Impaired voluntary quadriceps force control following anterior cruciate ligament reconstruction: relationship with knee function. *Knee Surgery, Sports Traumatology, Arthroscopy*, 25(5), 1424–1431. <https://doi.org/10.1007/s00167-015-3937-5>
- Pincivero, D. M., Coelho, A. J., & Campy, R. M. (2003). Perceived exertion and maximal quadriceps femoris muscle strength during dynamic knee extension exercise in young adult males and females. *European Journal of Applied Physiology*, 89(2), 150–156. <https://doi.org/10.1007/s00421-002-0768-0>
- Pinto, R. R., & Polito, M. D. (2016). Haemodynamic responses during resistance exercise with blood flow restriction in hypertensive subjects. *Clinical Physiology and Functional Imaging*, 36(5), 407–413. <https://doi.org/10.1111/cpf.12245>
- Poton, R., & Polito, M. D. (2016). Hemodynamic response to resistance exercise with and without blood flow restriction in healthy subjects. *Clinical Physiology and Functional Imaging*, 36(3), 231–236. <https://doi.org/10.1111/cpf.12218>
- Rossow, L. M., Fahs, C. A., Loenneke, J. P., Thiebaud, R. S., Sherk, V. D., Abe, T., & Bemben, M. G. (2012). Cardiovascular and perceptual responses to blood-flow-restricted resistance exercise with differing restrictive cuffs. *Clinical Physiology and Functional Imaging*, 32(5), 331–337. <https://doi.org/10.1111/j.1475-097X.2012.01131.x>
- Saka, T. (2014). Principles of postoperative anterior cruciate ligament rehabilitation. *World Journal of Orthopedics*, 5(4), 450. <https://doi.org/10.5312/wjo.v5.i4.450>
- Sardeli, A. V., Do Carmo Santos, L., Ferreira, M. L. V., Gáspari, A. F., Rodrigues, B., Cavaglieri, C. R., & Chacon-

- Mikahil, M. P. T. (2017). Cardiovascular Responses to Different Resistance Exercise Protocols in Elderly. *International Journal of Sports Medicine*, 38(12), 928–936. <https://doi.org/10.1055/s-0043-115737>
- Scott, B. R., Loenneke, J. P., Slattery, K. M., & Dascombe, B. J. (2015). Exercise with Blood Flow Restriction: An Updated Evidence-Based Approach for Enhanced Muscular Development. *Sports Medicine*, 45(3), 313–325. <https://doi.org/10.1007/s40279-014-0288-1>
- Segal, N. A., Williams, G. N., Davis, M. C., Wallace, R. B., & Mikesky, A. E. (2015). Efficacy of Blood Flow-Restricted, Low-Load Resistance Training in Women with Risk Factors for Symptomatic Knee Osteoarthritis. *PM and R*, 7(4), 376–384. <https://doi.org/10.1016/j.pmrj.2014.09.014>
- Segal, N., Davis, M. D., & Mikesky, A. E. (2015). Efficacy of Blood Flow-Restricted Low-Load Resistance Training For Quadriceps Strengthening in Men at Risk of Symptomatic Knee Osteoarthritis. *Geriatric Orthopaedic Surgery & Rehabilitation*, 6(3), 160–167. <https://doi.org/10.1177/2151458515583088>
- Shelbourne, K. D., & Trumper, R. V. (1997). Preventing Anterior Knee Pain After Anterior Cruciate Ligament Reconstruction. *The American Journal of Sports Medicine*, 25(1), 41–47. <https://doi.org/10.1177/036354659702500108>
- Staunton, C. A., May, A. K., Brandner, C. R., & Warmington, S. A. (2015). Haemodynamics of aerobic and resistance blood flow restriction exercise in young and older adults. *European Journal of Applied Physiology*, 115(11), 2293–2302. <https://doi.org/10.1007/s00421-015-3213-x>
- Suga, T., Okita, K., Morita, N., Yokota, T., Hirabayashi, K., Horiuchi, M., ... Tsutsui, H. (2009). Intramuscular metabolism during low-intensity resistance exercise with blood flow restriction. *Journal of Applied Physiology*, 106(4), 1119–1124. <https://doi.org/10.1152/jappphysiol.90368.2008>
- Suga, T., Okita, K., Takada, S., Omokawa, M., Kadoguchi, T., Yokota, T., ... Tsutsui, H. (2012). Effect of multiple set on intramuscular metabolic stress during low-intensity resistance exercise with blood flow restriction. *European Journal of Applied Physiology*, 112(11), 3915–3920. <https://doi.org/10.1007/s00421-012-2377-x>
- Tahami, S. M., & Rad, S. M. D. (2015). Outcome of ACL Reconstruction and Concomitant Articular Injury Treatment. *Archives of Bone and Joint Surgery*, 3(4), 260–263. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4628632/%5Chttp://www.ncbi.nlm.nih.gov/pmc/articles/PMC4628632/pdf/ABJS-3-260.pdf>
- Takano, H., Morita, T., Iida, H., Asada, K. ichi, Kato, M., Uno, K., ... Nakajima, T. (2005). Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. *European Journal of Applied Physiology*, 95(1), 65–73. <https://doi.org/10.1007/s00421-005-1389-1>
- Takarada, Y., Nakamura, Y., Aruga, S., Onda, T., Miyazaki, S., Ishii, N., ... Danielson, P. (2000). Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion restriction Rapid

- increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion, 61–65.
- Takarada, Y., Nozaki, D., & Taira, M. (2006). Force overestimation during tourniquet-induced transient occlusion of the brachial artery and possible underlying neural mechanisms. *Neuroscience Research*, 54(1), 38–42. <https://doi.org/10.1016/j.neures.2005.10.004>
- Takarada, Y., Sato, Y., & Ishii, N. (2002). Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. *European Journal of Applied Physiology*, 86(4), 308–314. <https://doi.org/10.1007/s00421-001-0561-5>
- Tennent, D. J., Hylden, C. M., Johnson, A. E., Burns, T. C., Wilken, J. M., & Owens, J. G. (2017). Blood flow restriction training after knee arthroscopy: A randomized controlled pilot study. *Clinical Journal of Sport Medicine*, 27(3), 245–252. <https://doi.org/10.1097/JSM.0000000000000377>
- Thomeé, R., Kaplan, Y., Kvist, J., Myklebust, G., Risberg, M. A., Theisen, D., ... Witvrouw, E. (2011). Muscle strength and hop performance criteria prior to return to sports after ACL reconstruction. *Knee Surgery, Sports Traumatology, Arthroscopy*, 19(11), 1798–1805. <https://doi.org/10.1007/s00167-011-1669-8>
- Tobalina, J. C., Calleja-González, J., De Santos, R. M., Fernández-López, J. R., & Arteaga-Ayarza, A. (2013). The effect of basketball footwear on the vertical ground reaction force during the landing phase of drop jumps. *Revista de Psicología Del Deporte*, 22(1), 179–182. <https://doi.org/10.1249/MSS.0b013e3181915670>
- Vieira, A., Gadelha, A. B., Ferreira-Junior, J. B., Vieira, C. A., de Melo Keene von Koenig Soares, E., Cadore, E. L., ... Bottaro, M. (2014). Session rating of perceived exertion following resistance exercise with blood flow restriction. *Clinical Physiology and Functional Imaging*, 35(5), 323–327. <https://doi.org/10.1111/cpf.12128>
- Vieira, P. J. C., Chiappa, G. R., Umpierre, D., Stein, R., & Ribeiro, J. P. (2013). Hemodynamic responses to resistance exercise with restricted blood flow in young and older men. *Journal of Strength and Conditioning Research*, 27(8), 2288–2294. <https://doi.org/10.1519/JSC.0b013e318278f21f>
- Wathan, D. (1994). Load assignment. In *Essentials of Strength Training and Conditioning* (pp. 435–439).
- Weatherholt, A., Beekley, M., Greer, S., Urtel, M., & Mikesky, A. (2013). Modified Kaatsu training: Adaptations and subject perceptions. *Medicine and Science in Sports and Exercise*, 45(5), 952–961. <https://doi.org/10.1249/MSS.0b013e31827ddb1f>
- Wernbom, M., Järrebring, R., Andreasson, M. A., & Augustsson, J. (2009). Acute effects of blood flow restriction on muscle activity and endurance during fatiguing dynamic knee extensions at low load. *Journal of Strength and Conditioning Research*, 23(8), 2389–2395. <https://doi.org/10.1519/JSC.0b013e3181bc1c2a>
- World Medical Association. (2013). World Medical Association declaration of Helsinki: Ethical principles for medical research involving human subjects. *Journal of American Medical Association*, 310(20), 2191–2194. <https://doi.org/10.1001/jama.2013.281053>

- Yasuda, T., Abe, T., Brechue, W. F., Iida, H., Takano, H., Meguro, K., ... Nakajima, T. (2010). Venous blood gas and metabolite response to low-intensity muscle contractions with external limb compression. *Metabolism: Clinical and Experimental*, 59(10), 1510–1519. <https://doi.org/10.1016/j.metabol.2010.01.016>
- Yasuda, T., Abe, T., Sato, Y., Midorikawa, T., Kearns, C. F., Inoue, K., ... Ishii, N. (2005). Muscle fiber cross-sectional area is increased after two weeks of twice daily KAATSU-resistance training. *International Journal of KAATSU Training Research*, 1(2), 65–70. <https://doi.org/10.3806/ijktr.1.65>
- Yasuda, T., Fujita, S., Ogasawara, R., Sato, Y., & Abe, T. (2010). Effects of low-intensity bench press training with restricted arm muscle blood flow on chest muscle hypertrophy: A pilot study. *Clinical Physiology and Functional Imaging*, 30(5), 338–343. <https://doi.org/10.1111/j.1475-097X.2010.00949.x>
- Yasuda, T., Fujita, T., Miyagi, Y., Kubota, Y., Sato, Y., Nakajima, T., ... Abe, T. (2006). Electromyographic responses of arm and chest muscle during bench press exercise with and without KAATSU. *International Journal of KAATSU Training Research*, 2(1), 15–18. <https://doi.org/10.3806/ijktr.2.15>
- Yasuda, T., Loenneke, J. P., Thiebaud, R. S., & Abe, T. (2012). Effects of Blood Flow Restricted Low-Intensity Concentric or Eccentric Training on Muscle Size and Strength. *PLoS ONE*, 7(12), 1–7. <https://doi.org/10.1371/journal.pone.0052843>
- Yasuda, T., Ogasawara, R., Sakamaki, M., Bembien, M. G., & Abe, T. (2011). Relationship between limb and trunk muscle hypertrophy following high-intensity resistance training and blood flow-restricted low-intensity resistance training. *Clinical Physiology and Functional Imaging*, 31(5), 347–351. <https://doi.org/10.1111/j.1475-097X.2011.01022.x>
- Yasuda, T., Ogasawara, R., Sakamaki, M., Ozaki, H., Sato, Y., & Abe, T. (2011). Combined effects of low-intensity blood flow restriction training and high-intensity resistance training on muscle strength and size. *European Journal of Applied Physiology*, 111(10), 2525–2533. <https://doi.org/10.1007/s00421-011-1873-8>

